Claims

1. Use of one or more double-stranded oligoribonucleotides (dsRNA) for the preparation of a composition for the specific modulation of the expression of one or more target genes in cells and/or tissues of the CNS and/or eye of a subject, wherein said composition is designed to be applied outside the blood-brain or blood-retina barriers.

2. A method for the specific modulation of the expression of target genes in cells and/or tissues of the CNS and/or eye, wherein a composition comprising one or more double-stranded oligoribonucleotides (dsRNA) is introduced into a cell, tissue or organism outside the blood-brain or blood-retina barriers.

3. The method of claim 2, wherein said method results in the provision of a test cell, test tissue or test organism, which can be preferably maintained under conditions allowing the degradation of the corresponding mRNA of one or more of target genes by RNA interference.

4. The method of claim 3 for the identification or validation of the function of a gene, further comprising comparing the resulting phenotype produced in the test cell, test tissue or test organism with that of a suitable control, thus allowing information on the function of the gene to be gained.

5. The use or method of any one of claims 1 to 4, wherein said specific modulation of the expression is an inhibition of target gene expression.

6. The use or method of any one of claims 1 to 5, wherein one or more of said target genes encode a cellular mRNA.

7. The use or method of any one of claims 1 or 6, wherein the cells and/or tissues are cells and/or tissues of the eye.

8. The use or method of any one of claims 1 to 7, wherein said cells or tissues are cells or tissues of the inner segment of the eye ball.

9. The use or method of claim 8, wherein said cells are retinal cells.

10. The use or method of claim 9, wherein said cells are cells of the retinal pigment epithelium (RPE) or neurosensory retina cells.

11. The use or method of any one of claims 1 to 10, wherein one or more of said target genes are predominantly expressed in said cell and/or tissue.

12. The use or method of any one of claims 1 to 11, wherein the expression of one or more of said target genes is specific for said cell and/or tissue.

13. The use or method of any one of claims 1 to 12, wherein said dsRNA molecules are between 21 and 23 nucleotides in length.

14. The use or method of any one of claims 1 to 13, wherein said dsRNA molecules contain a terminal 3'-hydroxyl group.

15. The use or method of any one of claims 1 to 14, wherein said dsRNA molecules have been chemically synthesized.

16. The use or method of any one of claims 1 to 15, wherein said dsRNA molecules represent an analogue of naturally occurring RNA.

17. The use or method of any one of claims 1 to 16, wherein said dsRNA analogues differ from the corresponding naturally occurring RNA by addition, deletion, substitution or modification of one or more nucleotides.

18. The use or method of any one of claims 1 to 17, wherein said dsRNA molecules inhibit the corresponding target genes by "posttranscriptional silencing".

19. The use or method of any one of claims 1 to 18, wherein said dsRNA molecules are encoded by a vector.

20. The use or method of any one of claims 19, wherein the expression said dsRNA is under control of a cell and/or tissue specific promoter.

21. The use or method of any one of claims 1 to 20, wherein the dsRNAs are introduced into the cells or tissues bound to other molecules and/or combined with one or more suitable carriers.

22. The use or method of claim 21, wherein the carrier is a micellar structure, preferably a liposome, a coat protein, derived from a virus such as the cytomegalovirus (CMV) or produced synthetically, adeno-associated virus (AAV) or adenovirus.

23. The use or method of claim 21 or 22, wherein the dsRNA is bound to cationic porphyrins, cationic polyamines, polymeric DNA-binding cations or fusogenic peptides.

24. The use or method of any one of claims 21 to 23, wherein the carrier and/or the dsRNA-binding molecules were selected such that the dsRNA molecules are delivered continuously to the target cells or target tissues over a defined period of time after application.

25. The use or method of any one of claims 21 to 24, wherein said carrier is specific for said cells and/or tissues as defined in any one of claims 7 to 12.

26. The use or method of any use of claims 1 to 25, wherein said composition is in form to be applied outside the eye ball, preferably by iontophoresis, retrobulbar or systemic application or as eye drops.

27. The use or method of any one of claims 1 to 25, wherein the subject or organism is a vertebrate.

28. The use or method of any one of claims 1 to 25, wherein the subject or organism is a mammal, preferably human.

29. The method of any one of claims 2 to 26, wherein the cells and/or tissues are of vertebrate origin.

30. The method of any one of claims 2 to 26 or 29, wherein the cells and/or tissues are of mammalian origin.

31. The method of claim 30, wherein the cells and/or tissues are of human origin.

32. A cell or tissue obtainable by a method of any one of claims 2 to 25 or 29 to 31, wherein the expression of a target genes is modulated.

33. An non-human organism obtainable by a method of any one of claims 2 to 27, comprising a cell or tissue of claim 32.

34. The organism of claim 33 which is a transgenic organism.

35. The organism of claim 33 or 34, wherein the organism displays the phenotype of an eye disease.

36. The organism of claim 35, wherein the organism displays the phenotype of a disease of the inner segment of the eye ball.

37. The organism of any one of claims 33 to 36, wherein the organism displays the phenotype of a retinal disease.

38. The organism of any one of claims 33 to 37, wherein the organism displays the phenotype of a degenerative retinal disease.

39. The organism of any one of claims 33 to 38 is a mouse, rat or zebra fish.

40. A pharmaceutical composition useful for the treatment of disease as defined in any one of claims 35 to 38, comprising a composition as defined in any one of claims 1 to 26.

41. A diagnostic composition for detecting a gene or gene expression involved in diseases of the CNS and/or eye, comprising a composition as defined in any one of claims 1 to 26, a cell or tissue of claim 32 or an organism of any one of claims 33 to 39.

42. A method of identification and isolation of a drug capable of specific modulation of the expression of a target gene in cells and/or tissues of the eye, comprising the steps:
(a) contacting a cell or tissue of claim 32 or a non-human organism of any one of claims 33 to 39 with a compound to be screened and;
(b) determining if the compound antagonizes or agonizes the effect of said one or more double-stranded oligoribonucleotides (dsRNA) molecules.

43. The method of claim 42, further comprising comparing the non-human organism treated with said compound with a non-treated control, wherein reversion or amelioration of the phenotype as defined in any one of claims 35 to 38 is indicative for a drug or lead compound for a drug for the treatment of a disease related to the eye.

44. Use of a component selected from the group consisting of a composition, nucleic acid, non-human organism, host cell, cell line, tissue, organ, drug, carrier and/or vector for the specific modulation of expression of one or more target genes in cells and/or tissue of the CNS and/or eye, wherein said component comprises one or more dsRNA molecules which are applicable outside the blood-brain barrier or the retinal region of the blood-retina barrier.

45. A kit for use in a method of any one of claims 2 to 27, 29 to 31, or 42 to 43, comprising at least one component as defined in claim 44.

46. The use of the method of any one of claims 2 to 31, cell of claim 32, or non-human organism of any one of claims 33 to 39 in drug discovery or target gene isolation and/or validation.

47. Use of RNA interference for the diagnosis and/or therapy of disorders related to the CNS and/or eye, or a nucleic acid, non-human organism, host cell, cell line, tissue, organ, carrier and/or vector for such use.